Brief Communication

Outcomes Management in a Real-World Evidence Context: The Case of Abiraterone and Enzalutamide in the Treatment of Metastatic Castration-Resistant Prostate Cancer

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ABSTRACT

At present, for patients with metastatic and castration-resistant prostate cancer, European Society for Medical Oncology and National Comprehensive Cancer Network guidelines recommend enzalutamide (E) or abiraterone (A). There are still a few studies comparing both drugs in a real-world setting, thus, in this article, we discuss an outcomes management methodology, supporting the follow-up of patients. This involves measuring relevant baseline traits and outcomes, such as overall survival (OS), treatment duration, patient-reported outcomes, and adverse events. We include 38 men in the A group and 15 in the E group. When comparing the survival of both drugs, both present similar OS. Regarding the quality-of-life analysis (QoL) with EPIC26, reported Standard QoL score was 58.3% in our patients, which was in line with the European Organization for the Research and Treatment of Cancer reference. As a result, by showing that we can capture the distinctive clinical benefits of A and E, and that patient-reported outcomes can be systematically collected for more than 2 years per living patient, we can now incorporate these findings in clinical discussions, risk-sharing agreements, or policy-level arguments.

Keywords: prostate cancer, enzalutamide, abiraterone

INTRODUCTION

Prostate cancer has the highest incidence rate in men in Portugal, accounting for 20% of all new diagnoses of cancer in men based on 2018 estimates.[1] In addition, mortality rates have remained steady for the past decade, at approximately 35%.[2] Worldwide, we can detect a similar trend, and prostate cancer is now the fifth leading cause of death from cancer in men.[3] It is expected that incidence will further increase by 80% until 2040.[3]

The guidelines of the European Society for Medical Oncology (ESMO) and of the National Comprehensive Cancer Network (NCCN) recommend enzalutamide (E) or abiraterone (A), for patients with metastatic and castration-resistant prostate cancer.[4,5] Abiraterone acetate is an antiandrogen drug used in combination with prednisone or prednisolone, and it has been approved in Portugal since 2016. Enzalutamide is also an antiandrogen and was also introduced in Portugal in 2016. There are not many studies directly comparing both drugs in a real-world setting. For example, a recent study by Shore et al.[6] concluded that both drugs have similar efficacy, but E has more adverse events than A. New randomized trials are now ongoing to access the efficacy and safety of both drugs when compared head-to-head.[7] Considering the rising importance of new payment schemes, for innovative drugs, like risk-sharing agreements, it is important to assess the outcomes of treatment in prostate cancer, in several settings/ perspectives, including hospitals. Health technology assessment analysis is also important, because these methodologies also can support the design of follow-up studies, namely by highlighting important variables and constructs to measure, because they are important for future decisions or to assess past decisions and possibly reevaluate strategies.

At present, for patients with metastatic and castration-resistant prostate cancer, ESMO and NCCN guidelines recommend E or A. There are still a few studies

Table 1.—Baseline characteristics of the population

Clinical Characteristics	Abiraterone		Enzalutamide	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Stage at diagnosis				
IIIb	1	2.60	1	6.70
IV	37	97.40	14	93.3
Histologic grade (G) at diagnosis				
G2 moderately differentiated	3	7.90	1	6.70
G3 poorly differentiated	35	92.10	14	93.3
Gleason score at diagnosis				
6	3	7.90	1	6.70
7	13	34.20	8	53.3
8	6	15.80	3	20.0
9	11	28.90	2	13.3
10	5	13.20	1	6.70
ECOG baseline				
ECOG 0	22	57.90	7	46.7
ECOG 1	14	36.80	4	26.7
ECOG 2	2	5.30	3	20.0
ECOG 3	0	0.00	1	6.7
Therapeutic line				
1st	1	2.60	1	6.7
2nd	17	44.70	9	60.0
3rd	14	36.80	3	20.0
4th and following	6	15.80	2	13.3

ECOG, Eastern Cooperative Oncology Group.

comparing both drugs in a real-world setting, thus, in this article, we discuss an outcomes management methodology, supporting the follow-up of patients. This involves measuring relevant baseline traits and outcomes, such as overall survival (OS), treatment duration, patient-reported outcomes, and adverse events.

Objective

We discuss an outcomes management methodology, supporting the follow-up of patients. This involves, namely, (1) measuring relevant baseline traits and (2) outcomes such as OS, treatment duration, patient-reported outcomes, and adverse events. This research empirically reports the case of patients with metastatic castration-resistant cancer, using A or E. Our primary objective was to compare the survival of both groups and the adverse events profile As a secondary objective, we wanted to measure the reported QoL of our patients.

METHODS

This is a retrospective observational study. A convenient dataset, collected for the purpose of illustrating the methodology, includes all appropriate patients undergoing treatment with A or E, from 2012 to 2019. Data were collected at a hospital-based, electronic health record of Luz Saúde, Portugal. The data were obtained from the main clinical file system and also collected from pharmaceutical consultations that took place at the dispensing of the drugs. Baseline characteristics included age, staging, Eastern Cooperative Oncology Group (ECOG) Performance Status, Gleason score, histology, duration of treatment, and survival. Statistical analysis was performed with SPSS V23.0 (IBM Corp., Armonk, NY) for OS analysis with Kaplan-Meier Curves. To assess for the need of adjustment of confounders, we performed two-tailed analysis of variance tests and describe both the *f*-value and *p*-value. QoL data at Luz Saúde were captured with the use of EPIC26 for prostate cancer, a digital composite score that allows evaluation of each QoL dimension using a numerical scale. For symptoms and difficulties, lower scores mean better status, for capacities, higher scores are desired.

All adult patients with at least one drug dispensed (A or E) were included. Concomitant chronic disease was accepted in this study. Patients without baseline information (three patients) or with an inconsistent QoL EPIC26 questionnaire (one patient) were excluded. We also excluded patients with more than one type of cancer.

We analyzed clinical outcomes that are important for the patients: OS as the primary outcome and QoL as a secondary outcome. We collected the baseline variables to use them to explain variation of outcomes, should it arise in the analysis. Accordingly, all decisions affecting these variables must be taken in advance, so that the registration routines are set in place in the due time.

RESULTS

We included 38 men in the A group and 15 in the E group, with a median age at diagnosis of 69 years (interquartile range 47–78). At diagnosis, more than 97%

Table 2.—Outcomes

	Abiraterone	Enzalutamide
No. of patients	38	15
Median treatment duration, mo	6.5	4.3
(95% confidence interval)	(5.14–7.86)	(1.58–7.02)
Overall survival, mo	16.7	17.1
Adverse events (% patients)	17 (45)	8 (53)
Discontinuations due to adverse events, %	5	13
Most common adverse events, n (%)		
Tiredness	3 (20)	3 (38)
Nausea and vomiting	2 (12)	3 (38)
Diarrhea	2 (12)	1 (13)

of patients, in both groups, presented a stage IV disease, all of them with at least one bone metastasis. A and E were used especially in second and third therapeutic lines, and most patients had an ECOG of 0 or 1. In both in A and E groups, a large proportion of patients had a Gleason score of 7: 34.2% and 57.9%, respectively. Also, in both groups, a vast majority of patients had a poorly differentiated (G3) histologic classification. These data are summarized in Table 1.

When comparing the survival of both drugs, they present similar OS, but the median duration of treatment was higher in the A group. The primary outcomes comparison between the two groups is detailed in Table 2. We found no significant difference in outcomes. Regression analysis shows that the variation on OS, both in the case of A and E, is not explained by variation on the independent variables Gleason and ECOG, even for *p*-value 0.05 (Table 3).

Regarding the QoL analysis with EPIC26, reported Standard QoL score (SQL) is 58.3% in our patients, whereas the European Organization for the Research and Treatment of Cancer (EORTC) reference[8] for these group of patients is 62.1%. The symptom burden in our patients is lower than the reference for pain, nausea and vomiting, and fatigue. The comparison of our scores with the EORTC reference is detailed in Figure 1, which compares our results with the reference in each dimension of the QoL composite index.

DISCUSSION AND LIMITATIONS

Considering the lack of head-to-head real-world comparisons of A versus E, this is an important study.

Table 3.—Statistical analysis of baseline traits effect on the overall survival

	Abiraterone		Enzalutamide	
Statistical Parameter	**ECOG PS**	**Gleason**	**ECOG PS**	**Gleason**
F-test significance	0.0612		0.052	
T-test (*p*-value)	0.119	0.064	0.81	0.352

ECOG PS, Eastern Cooperative Oncology Group Performance Status.

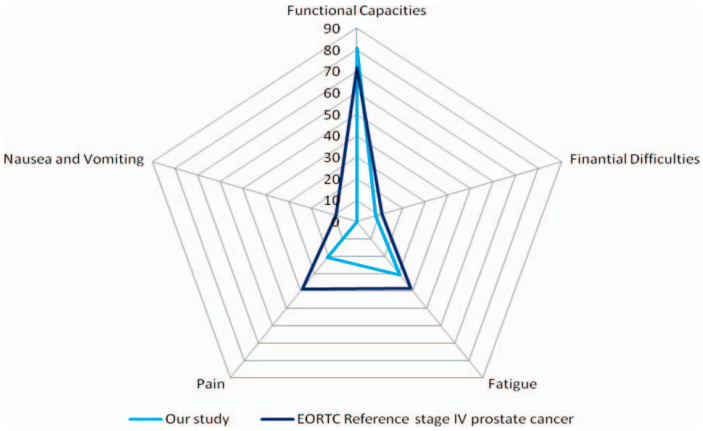

Figure 1.—Comparison between observed quality-of-life scores and the EORTC reference values in each studied dimension. EORTC, European Organization for the Research and Treatment of Cancer.

We access the survival and tolerability of both drugs and include a QoL evaluation of the total sample of patients. As found in previous clinical studies, the survival is similar between A and E, with a difference on the AE profile. Despite this, there are limitations that reduce the external power of our findings: this is a unicentric study, with a small sample. Also, we could not gather enough data to do the QoL comparison between A and E, which would be important to assess the differential benefit of each drug.

We also investigated the role of baseline variables at explaining the difference between the outcomes of A and E. Considering that OS variation was not explained by the independent variables (ie, the baselines), they can be attributed to the different interventions (treatments A and E). We highlight these steps because they are important methodological check points, and this article aims at contributing on establishing steps and methods to implement real-world studies in a hospital setting.

We included 38 men in the A group and 15 in the E group. When comparing the survival of both drugs, both present similar OS. Regarding the QoL analysis with EPIC26, reported SQL score was 58.3% in our patients, which was in line with the EORTC reference. As a result, by showing that we can capture the distinctive clinical benefits of A and E , and that patient-reported outcomes can be systematically collected for more than 2 years per living patient, we can now incorporate these findings in clinical discussions, risk-sharing agreements, or policy-level arguments.

CONCLUSIONS

We conclude that in our setting there are no significant differences in real-world use of A and E. This may have important implications for both our clinical practice and in the negotiation with our suppliers. Also, this will reinforce the capabilities of the proposed methodology for doing proper follow-up and discrimination among the findings. As a result, we are able to

show that we can capture the distinctive clinical benefits of A and E, and that patient-reported outcomes can be systematically collected for more than 2 years per living patient. We can now incorporate these findings in clinical discussions and at company policy-level definition. The objective of providing an illustration of our methodology for data collection is achieved.

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